Pharma industry: quality assurance or quality management?

Julia Sipos

Institute of Isotopes Co. Ltd., Hungary

Historical background and evolution

- GMP's history started in early 1900s
- Formailsed regulation since 1963
- Focused on patient safety and product quality
- Starting point to change of approach: Issue of ISO 9001:2000 and related documents
  - quality management instead of quality assurance
  - use of PDCA cycle
  - planned for integrated use with other systems
  - eight quality principles…

Eight quality principles

- Customer focus
- Leadership
- Involvement of people
- Process approach
- System approach to management
- Continual improvement
- Factual approach to decision making
- Mutually beneficial supplier relationships

Terms and definitions - ISO 9000:2005

- Quality management

  coordinated activities to direct and control an organization with regard to quality. It includes:
  - establishment of the quality policy and quality objectives,
  - quality planning
  - quality control
  - quality assurance and
  - quality improvement
- Quality assurance

  focused on providing confidence that quality requirements will be fulfilled.

New approach in pharma legislation

- Quality Management System for APIs Manufacturers – integrating ICH Q7 into ISO 9001 (September, 2005)

  „…ISO 9001:200series are an excellent complementary fit to the GMP requirements…"

- Pharmaceutical Quality System – ICH Q10 (June, 2008, latest issue: January, 2011)

  „…an example of a pharmaceutical quality system designed for the entire product lifecycle and therefore goes beyond current GMP requirements"

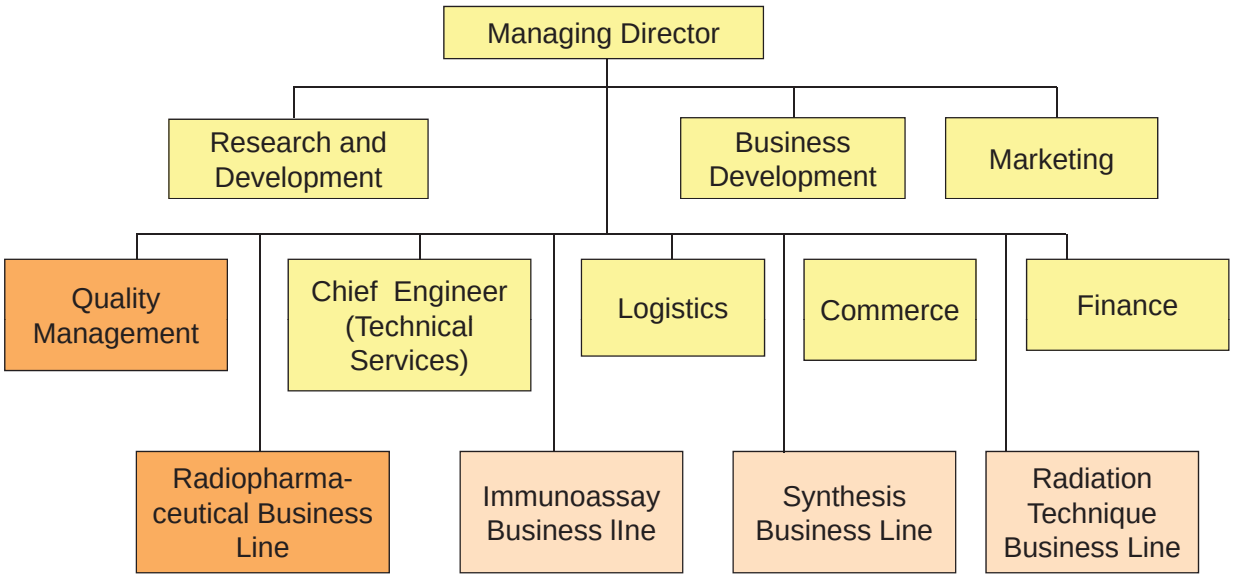
Latest issues

- Changes of Chapter 4 an Annex 11 of GMP guide
  - due to spread of computer systems
  - structure and content integrates ISO 9001 requirements
- Discussion opened about change of Chapter 8
  - „Concept paper on Revising Chapter 8 of the EC guide to GMP to introduce risk-based concepts and to provide for more effective investigations and CAPA actions"

Institute of Isotopes Co. Ltd

- Institute of Isotopes was established in 1959 by the Hungarian Atomic Energy Committee
- New organizational system from 1993 – devided in three independent organisations
  - ***Institute of Isotopes Co., Ltd.***
  - Institute of Isotopes (research institute)
  - Izinta Co., Ltd. (trading company)
- Export rate above 75% to more than 60 countries, more than 120 customers

Organization



Number of employees: total ~ 180, in pharma: ~ 35 (production & QC)

Infrastructure and licences

- Laboratories
  - Total area (in whole company): ~10 000 m^2
  - Laboratories for treatment of radioactivity of high & medium level
  - Clean rooms for production of non-radioactive and radioactive pharmaceutical production
- Licensed company, possessing a GMP Certificate for
  - pharmaceutical preparation
  - manufacturing of APIs
  - investigational products for clinical trials

Radiopharmaceutical Business Line Products

- „In vivo" tracers – small quantities, special radioactive products
- Cold kits for ^{99m}Tc-labelling for diagnostic purposes:
  - kidney (scintigraphy - DMSA, glomerular & tubular function - DTPA & EC)
  - liver and hepatobiliary system (morphology - FYTON, function - TECHIDA)
  - bone scintigraphy, metastasis localization - MDP
- Standard reactor isotopes produced: ^{125}I, ^{131}I, ^{90}Y, ^{153}Sm, ^{166}Ho
- Most important radiopharmaceuticals
  - ^{131}I solution and capsule – for treatment of hyperthyreosis and thyroid carcinoma
  - ^{131}I MIBG - for diagnosis and treatment of neuroendocrine tumours
  - ^{90}Y and ^{153}Sm for labelling MULTIBONE-kit – for treatment of painful bone metastases
  - ^{166}Ho for labelling SYNOPHYT kit – for treatment of rheumatoid arthritis in the knee
  - ^{14}C-urea capsule – for a breath test for diagnosis of Helicobacter pylori infection

History of QMSs at the company

- First implementation of ISO 9001 QMS
  - for all activities of the company (including pharmaceuticals)
  - certified in 1998
  - according to ISO 9001:1994
  - central and business line level documents
  - separate and very detailed regulations in all areas
- Results
  - operation
    - became more regulated
    - could be followed more easily, but it „caused" …
- Difficulties
  - to keep the system up-to-date and
  - in some cases unnecessary/duplicate documentation to be done
- Upgrade to ISO 9001:2000 – was not so fundamental as it could be due to the new approach of the standard

History of QMSs at the company

- Implementation of GMP regulations for pharmaceutical aspects
  - in some cases existing documents were amended, but
  - in most cases additional documents were established

  where regulation was missing
- National Authority's inspections (after upgrade to EU-requirements): 2002, 2005 and 2008, 2011
  - preferred to handle GMP as separate as possible from ISO 9001 QMS (2002-2008)
  - the integrated thinking was more accepted in 2011

History of QMSs at the company

- For in vitro diagnostics: certified ISO 13485 quality management system
  - since 2008 for one product
  - since 2009 for all IVDs for human healthcare use
- CE mark for IVDs according to EU regulations including those requiring certification (PSA tumour markers)
- Fully integrated system with ISO 9001
- Number of new regulations is very limited
  - procedure for additional requirements (e.g. handling of technical documentation)
  - cross reference table (essential requirements vs. QMS)

Improvement of QMS

- Change to more user friendly system is now in process for all activities of the company
- Main challenges:
  - change way of thinking about systems integration
  - handling impact of changes on the whole system
- No company level computerised management system in place (partial systems are available)
  - so far we improved the system within current possibilities
  - now it is planned to be implemented
- In order to make the operation more
  - integrated and so
  - effective and efficient

Improvement of QMS

- Taking into account specialities of the company
  - small industry
  - national company
  - special product nature (radioactive)
- PDCA to be followed in each activity, e.g.
  - preparation to new activities
  - handling of deviations, CAPAs
  - handling of change control
- Application of risk assessment in planning of
  - re-validation and re-qualification frequency
  - training
  - self-inspection (internal audit)
  - supplier audit

Improvement of QMS

- To update documentation to make it more
  - transparent
  - easy to use
  - easy to update
- System improvement is a
  - step by step process
  - a planned and controlled activity
- The system integrity shall be maintained for all activities during improvement period throughout the company
- The improvement supports awareness of employees

Achievements so far – since 2009

- Risk assessment systematically used
- Handling of documentation (both prescriptions and records) updated
- Centralised registry and database established for
  - handling of deviations and „ISO nonconformities" (CAPA)
  - change controls
  - out of specification results
- Process of logistics (excluding production and sales) updated in unified manner
- Complaints and CAPA handling procedure updated
- Sampling SOPs updated and simplified in structure

Further plans

- Update design and development procedure
- Update and simplification SOP level regulations (e.g. in maintenance)
- To be involved in implementation of computerised management system in order to
  - take part in fundamental changes that impact QMSs
  - have an early understanding of requirements and opportunities
  - speed up improvement process of GMP compliance in a user friendly manner

Ultimate result: movement from management of quality towards quality of management

THANK YOU FOR YOUR ATTENTION!

www.izotop.hu
izotop@izotop.hu